

SEQUENCE LISTING

<110> Solari, Roberto Celeste Ercole
Champion, Brian Robert
Ward, George Albert

<120> Conjugate of a Transport Protein and a Protein for Modulation
of Notch Signalling

<130> 674525-2007

<140> 2003-11-25

<141> To be assigned

<150> 2002-05-24

<151> PCT/GB02/02438

<150> 2001-05-25

<151> GB 0112818.0

<160> 13

<170> PatentIn version 3.1

<210> 1

<211> 29

<212> DNA

<213> Artificial sequence

<220>

<221> PCR primer for amplifying HES1 promoter from mouse genomic DNA

<400> 1

ggggtaccct caggcgcgcg ccattggcc 29

<210> 2

<211> 29

<212> DNA

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<400> 2

gaagatctgc ttacgtcctt ttacttgac 29

<210> 3

<211> 26

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<221> Adenovirus major late promoter TATA-box motif with BglIII and
HindIII cohesive ends

<400> 3

gatctggggg gctataaaag ggggta 26

<210> 4
 <211> 26
 <212> DNA
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 <400> 4
 acccccgat attttccccc attcga 26

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 <211> 61
 <212> DNA
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 <221> CBF-1 promoter tetramer with XhoI and BglII cohesive ends

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 a 61

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 <212> DNA
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 <221> CBF-1 promoter tetramer with XhoI and BglII cohesive ends

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 <212> DNA
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 <221> PCR amplimer for generating a truncated fragment of human Notch1 cDNA

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 <210> 8
 <211> 31
 <212> DNA
 <213> Artificial sequence
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 <221> PCR amplimer for generating a truncated fragment of human

Notch1 cDNA

<400> 8
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<211> 91
<212> DNA
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<221> Oligo annealed to the NIC2202 sequence to remove the stop
codon from theNIC2202 fragment of human Notch1 cDNA

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cctggcctgt ggaagcaagg agccaagga cctcaaggca cggaggaaga agtcccagga 60
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codon from theNIC2202 fragment of human Notch1 cDNA

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accgttcccg acggacgacc tgccgccggc gagct 95

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<222> (891)..(892)
<223> x = any amino acid

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20 25 30

Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys

35

40

45

Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu
 50 55 60

Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg
 65 70 75 80

Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro
 85 90 95

Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg
 100 105 110

Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg
 115 120 125

Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys
 130 135 140

Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala
 145 150 155 160

Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg
 165 170 175

Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly
 180 185 190

Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala
 195 200 205

Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro
 210 215 220

Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr
 225 230 235 240

His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu
 245 250 255

Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys
 260 265 270

Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr
275 280 285

Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn
290 295 300

Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn
305 310 315 320

Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile
325 330 335

Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp
340 345 350

Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu
355 360 365

Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly
370 375 380

Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys
385 390 395 400

Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys
405 410 415

Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr
420 425 430

Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg
435 440 445

Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp
450 455 460

Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro
465 470 475 480

Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser
485 490 495

Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe
500 505 510

Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp
515 520 525

Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu
530 535 540

Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly
545 550 555 560

Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His
565 570 575

Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg
580 585 590

Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser
595 600 605

Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala
610 615 620

Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile
625 630 635 640

Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu
645 650 655

Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly
660 665 670

Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His
675 680 685

Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys
690 695 700

Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys
705 710 715 720

Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly
725 730 735

Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
740 745 750

Asn Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
755 760 765

Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser
770 775 780

Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys
785 790 795 800

Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn
805 810 815

Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro
820 825 830

Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu
835 840 845

Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly
850 855 860

Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg
865 870 875 880

His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys
885 890 895

Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys
900 905 910

Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn
915 920 925

Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu
930 935 940

Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn

945

950

955

960

Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe
 965 970 975

Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser
 980 985 990

Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys
 995 1000 1005

Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val
 1010 1015 1020

Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln
 1025 1030 1035

Asp Gly Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr
 1040 1045 1050

Gly Pro Asn Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro
 1055 1060 1065

Cys Lys Asn Gly Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg
 1070 1075 1080

Cys Glu Cys Pro Ser Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro
 1085 1090 1095

Ser Val Ser Cys Glu Val Ala Ala Gln Arg Gln Gly Val Asp Val
 1100 1105 1110

Ala Arg Leu Cys Gln His Gly Gly Leu Cys Val Asp Ala Gly Asn
 1115 1120 1125

Thr His His Cys Arg Cys Gln Ala Gly Tyr Thr Gly Ser Tyr Cys
 1130 1135 1140

Glu Asp Leu Val Asp Glu Cys Ser Pro Ser Pro Cys Gln Asn Gly
 1145 1150 1155

Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr Ser Cys Lys Cys Val
 1160 1165 1170

Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu Ile Asp Glu Cys
1175 1180 1185

Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu Asp Leu Pro
1190 1195 1200

Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly Val His
1205 1210 1215

Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro Val
1220 1225 1230

Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln
1235 1240 1245

Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu
1250 1255 1260

Arg Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp
1265 1270 1275

Ala Arg Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His
1280 1285 1290

Cys Glu Cys Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val
1295 1300 1305

Ile Asn Gly Cys Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys
1310 1315 1320

Ala Val Ala Ser Asn Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro
1325 1330 1335

Ala Gly Phe Glu Gly Ala Thr Cys Glu Asn Asp Ala Arg Thr Cys
1340 1345 1350

Gly Ser Leu Arg Cys Leu Asn Gly Gly Thr Cys Ile Ser Gly Pro
1355 1360 1365

Arg Ser Pro Thr Cys Leu Cys Leu Gly Pro Phe Thr Gly Pro Glu
1370 1375 1380

Cys Gln Phe Pro Ala Ser Ser Pro Cys Leu Gly Gly Asn Pro Cys
1385 1390 1395

Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser Glu Ser Pro Phe Tyr
1400 1405 1410

Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu Leu Cys His Ile
1415 1420 1425

Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp Ile Pro Pro
1430 1435 1440

Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln Glu Asp
1445 1450 1455

Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala Cys
1460 1465 1470

Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp
1475 1480 1485

Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp
1490 1495 1500

Gly His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp
1505 1510 1515

Gly Phe Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr
1520 1525 1530

Asp Gln Tyr Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln
1535 1540 1545

Gly Cys Asn Ser Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala
1550 1555 1560

Glu His Val Pro Glu Arg Leu Ala Ala Gly Thr Leu Val Val Val
1565 1570 1575

Val Leu Met Pro Pro Glu Gln Leu Arg Asn Ser Ser Phe His Phe
1580 1585 1590

Leu Arg Glu Leu Ser Arg Val Leu His Thr Asn Val Val Phe Lys
1595 1600 1605

Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg
1610 1615 1620

Glu Glu Glu Leu Arg Lys His Pro Ile Lys Arg Ala Ala Glu Gly
1625 1630 1635

Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln Val Lys Ala Ser Leu
1640 1645 1650

Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg Arg Glu Leu Asp
1655 1660 1665

Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu Ile Asp Asn
1670 1675 1680

Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser Ala Thr
1685 1690 1695

Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser Leu
1700 1705 1710

Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu
1715 1720 1725

Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala
1730 1735 1740

Ala Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser
1745 1750 1755

Arg Lys Arg Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly
1760 1765 1770

Phe Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu
1775 1780 1785

Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp
1790 1795 1800

Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp

1805		1810		1815
Leu Glu Thr Lys Lys Phe Arg	Phe Glu Glu Pro Val	Val Leu Pro		
1820	1825	1830		
Asp Leu Asp Asp Gln Thr Asp	His Arg Gln Trp Thr	Gln Gln His		
1835	1840	1845		
Leu Asp Ala Ala Asp Leu Arg	Met Ser Ala Met Ala	Pro Thr Pro		
1850	1855	1860		
Pro Gln Gly Glu Val Asp Ala	Asp Cys Met Asp Val	Asn Val Arg		
1865	1870	1875		
Gly Pro Asp Gly Phe Thr Pro	Leu Met Ile Ala Ser	Cys Ser Gly		
1880	1885	1890		
Gly Gly Leu Glu Thr Gly Asn	Ser Glu Glu Glu Glu	Asp Ala Pro		
1895	1900	1905		
Ala Val Ile Ser Asp Phe Ile	Tyr Gln Gly Ala Ser	Leu His Asn		
1910	1915	1920		
Gln Thr Asp Arg Thr Gly Glu	Thr Ala Leu His Leu	Ala Ala Arg		
1925	1930	1935		
Tyr Ser Arg Ser Asp Ala Ala	Lys Arg Leu Leu Glu	Ala Ser Ala		
1940	1945	1950		
Asp Ala Asn Ile Gln Asp Asn	Met Gly Arg Thr Pro	Leu His Ala		
1955	1960	1965		
Ala Val Ser Ala Asp Ala Gln	Gly Val Phe Gln Ile	Leu Ile Arg		
1970	1975	1980		
Asn Arg Ala Thr Asp Leu Asp	Ala Arg Met His Asp	Gly Thr Thr		
1985	1990	1995		
Pro Leu Ile Leu Ala Ala Arg	Leu Ala Val Glu Gly	Met Leu Glu		
2000	2005	2010		
Asp Leu Ile Asn Ser His Ala	Asp Val Asn Ala Val	Asp Asp Leu		
2015	2020	2025		

Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp
2030 2035 2040

Ala Ala Val Val Leu Leu Lys Asn Gly Ala Asn Lys Asp Met Gln
2045 2050 2055

Asn Asn Arg Glu Glu Thr Pro Leu Phe Leu Ala Ala Arg Glu Gly
2060 2065 2070

Ser Tyr Glu Thr Ala Lys Val Leu Leu Asp His Phe Ala Asn Arg
2075 2080 2085

Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp Ile Ala Gln
2090 2095 2100

Glu Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu Tyr Asn
2105 2110 2115

Leu Val Arg Ser Pro Gln Leu His Gly Ala Pro Leu Gly Gly Thr
2120 2125 2130

Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn Gly Tyr Leu Gly
2135 2140 2145

Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg Lys Pro Ser
2150 2155 2160

Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp Leu Lys
2165 2170 2175

Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu Asp
2180 2185 2190

Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His
2195 2200 2205

Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro
2210 2215 2220

Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met
2225 2230 2235

Pro Asp Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys
2240 2245 2250

Pro Glu Met Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu
2255 2260 2265

Thr Gly Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr
2270 2275 2280

Ser Thr Val Leu Gly Ser Ser Ser Gly Gly Ala Leu Asn Phe Thr
2285 2290 2295

Val Gly Gly Ser Thr Ser Leu Asn Gly Gln Cys Glu Trp Leu Ser
2300 2305 2310

Arg Leu Gln Ser Gly Met Val Pro Asn Gln Tyr Asn Pro Leu Arg
2315 2320 2325

Gly Ser Val Ala Pro Gly Pro Leu Ser Thr Gln Ala Pro Ser Leu
2330 2335 2340

Gln His Gly Met Val Gly Pro Leu His Ser Ser Leu Ala Ala Ser
2345 2350 2355

Ala Leu Ser Gln Met Met Ser Tyr Gln Gly Leu Pro Ser Thr Arg
2360 2365 2370

Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln Val Gln Pro
2375 2380 2385

Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro Ala Asn Ile
2390 2395 2400

Gln Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro Gln Pro
2405 2410 2415

His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg Ser
2420 2425 2430

Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val Gln Pro Leu Gly
2435 2440 2445

Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln Glu Ser Pro
2450 2455 2460

Ala Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro Val Thr
2465 2470 2475

Ala Ala Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser
2480 2485 2490

Pro Val Asp Asn Thr Pro Ser His Gln Leu Gln Val Pro Glu His
2495 2500 2505

Pro Phe Leu Thr Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser
2510 2515 2520

Ser Ser Pro His Ser Asn Val Ser Asp Trp Ser Glu Gly Val Ser
2525 2530 2535

Ser Pro Pro Thr Ser Met Gln Ser Gln Ile Ala Arg Ile Pro Glu
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Ala Phe Lys
2555

<210> 12
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<212> PRT
<213> Homo sapiens

<400> 12

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20 25 30

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35 40 45

Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His
50 55 60

Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val
65 70 75 80

Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe
85 90 95

Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser
100 105 110

Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr
115 120 125

Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp
130 135 140

Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr
145 150 155 160

Thr Val Ala Asn Gln Phe Ser Cys Lys Cys Leu Thr Gly Phe Thr Gly
165 170 175

Gln Lys Cys Glu Thr Asp Val Asn Glu Cys Asp Ile Pro Gly His Cys
180 185 190

Gln His Gly Gly Thr Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln
195 200 205

Cys Pro Gln Gly Phe Thr Gly Gln Tyr Cys Asp Ser Leu Tyr Val Pro
210 215 220

Cys Ala Pro Ser Pro Cys Val Asn Gly Gly Thr Cys Arg Gln Thr Gly
225 230 235 240

Asp Phe Thr Phe Glu Cys Asn Cys Leu Pro Gly Phe Glu Gly Ser Thr
245 250 255

Cys Glu Arg Asn Ile Asp Asp Cys Pro Asn His Arg Cys Gln Asn Gly
260 265 270

Gly Val Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro
275 280 285

Gln Trp Thr Gly Gln Phe Cys Thr Glu Asp Val Asp Glu Cys Leu Leu
290 295 300

Gln Pro Asn Ala Cys Gln Asn Gly Gly Thr Cys Ala Asn Arg Asn Gly
305 310 315 320

Gly Tyr Gly Cys Val Cys Val Asn Gly Trp Ser Gly Asp Asp Cys Ser
325 330 335

Glu Asn Ile Asp Asp Cys Ala Phe Ala Ser Cys Thr Pro Gly Ser Thr
340 345 350

Cys Ile Asp Arg Val Ala Ser Phe Ser Cys Met Cys Pro Glu Gly Lys
355 360 365

Ala Gly Leu Leu Cys His Leu Asp Asp Ala Cys Ile Ser Asn Pro Cys
370 375 380

His Lys Gly Ala Leu Cys Asp Thr Asn Pro Leu Asn Gly Gln Tyr Ile
385 390 395 400

Cys Thr Cys Pro Gln Gly Tyr Lys Gly Ala Asp Cys Thr Glu Asp Val
405 410 415

Asp Glu Cys Ala Met Ala Asn Ser Asn Pro Cys Glu His Ala Gly Lys
420 425 430

Cys Val Asn Thr Asp Gly Ala Phe His Cys Glu Cys Leu Lys Gly Tyr
435 440 445

Ala Gly Pro Arg Cys Glu Met Asp Ile Asn Glu Cys His Ser Asp Pro
450 455 460

Cys Gln Asn Asp Ala Thr Cys Leu Asp Lys Ile Gly Gly Phe Thr Cys
465 470 475 480

Leu Cys Met Pro Gly Phe Lys Gly Val His Cys Glu Leu Glu Ile Asn
485 490 495

Glu Cys Gln Ser Asn Pro Cys Val Asn Asn Gly Gln Cys Val Asp Lys
500 505 510

Val Asn Arg Phe Gln Cys Leu Cys Pro Pro Gly Phe Thr Gly Pro Val
515 520 525

Cys Gln Ile Asp Ile Asp Asp Cys Ser Ser Thr Pro Cys Leu Asn Gly
530 535 540

Ala Lys Cys Ile Asp His Pro Asn Gly Tyr Glu Cys Gln Cys Ala Thr
545 550 555 560

Gly Phe Thr Gly Val Leu Cys Glu Glu Asn Ile Asp Asn Cys Asp Pro
565 570 575

Asp Pro Cys His His Gly Gln Cys Gln Asp Gly Ile Asp Ser Tyr Thr
580 585 590

Cys Ile Cys Asn Pro Gly Tyr Met Gly Ala Ile Cys Ser Asp Gln Ile
595 600 605

Asp Glu Cys Tyr Ser Ser Pro Cys Leu Asn Asp Gly Arg Cys Ile Asp
610 615 620

Leu Val Asn Gly Tyr Gln Cys Asn Cys Gln Pro Gly Thr Ser Gly Val
625 630 635 640

Asn Cys Glu Ile Asn Phe Asp Asp Cys Ala Ser Asn Pro Cys Ile His
645 650 655

Gly Ile Cys Met Asp Gly Ile Asn Arg Tyr Ser Cys Val Cys Ser Pro
660 665 670

Gly Phe Thr Gly Gln Arg Cys Asn Ile Asp Ile Asp Glu Cys Ala Ser
675 680 685

Asn Pro Cys Arg Lys Gly Ala Thr Cys Ile Asn Gly Val Asn Gly Phe
690 695 700

Arg Cys Ile Cys Pro Glu Gly Pro His His Pro Ser Cys Tyr Ser Gln
705 710 715 720

Val Asn Glu Cys Leu Ser Asn Pro Cys Ile His Gly Asn Cys Thr Gly
725 730 735

Gly Leu Ser Gly Tyr Lys Cys Leu Cys Asp Ala Gly Trp Val Gly Ile
740 745 750

Asn Cys Glu Val Asp Lys Asn Glu Cys Leu Ser Asn Pro Cys Gln Asn

755

760

765

Gly Gly Thr Cys Asp Asn Leu Val Asn Gly Tyr Arg Cys Thr Cys Lys
 770 775 780

Lys Gly Phe Lys Gly Tyr Asn Cys Gln Val Asn Ile Asp Glu Cys Ala
 785 790 795 800

Ser Asn Pro Cys Leu Asn Gln Gly Thr Cys Phe Asp Asp Ile Ser Gly
 805 810 815

Tyr Thr Cys His Cys Val Leu Pro Tyr Thr Gly Lys Asn Cys Gln Thr
 820 825 830

Val Leu Ala Pro Cys Ser Pro Asn Pro Cys Glu Asn Ala Ala Val Cys
 835 840 845

Lys Glu Ser Pro Asn Phe Glu Ser Tyr Thr Cys Leu Cys Ala Pro Gly
 850 855 860

Trp Gln Gly Gln Arg Cys Thr Ile Asp Ile Asp Glu Cys Ile Ser Lys
 865 870 875 880

Pro Cys Met Asn His Gly Leu Cys His Asn Thr Gln Gly Ser Tyr Met
 885 890 895

Cys Glu Cys Pro Pro Gly Phe Ser Gly Met Asp Cys Glu Glu Asp Ile
 900 905 910

Asp Asp Cys Leu Ala Asn Pro Cys Gln Asn Gly Gly Ser Cys Met Asp
 915 920 925

Gly Val Asn Thr Phe Ser Cys Leu Cys Leu Pro Gly Phe Thr Gly Asp
 930 935 940

Lys Cys Gln Thr Asp Met Asn Glu Cys Leu Ser Glu Pro Cys Lys Asn
 945 950 955 960

Gly Gly Thr Cys Ser Asp Tyr Val Asn Ser Tyr Thr Cys Lys Cys Gln
 965 970 975

Ala Gly Phe Asp Gly Val His Cys Glu Asn Asn Ile Asn Glu Cys Thr
 980 985 990

Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser
995 1000 1005

Phe Ser Cys Leu Cys Pro Val Gly Phe Thr Gly Ser Phe Cys Leu
1010 1015 1020

His Glu Ile Asn Glu Cys Ser Ser His Pro Cys Leu Asn Glu Gly
1025 1030 1035

Thr Cys Val Asp Gly Leu Gly Thr Tyr Arg Cys Ser Cys Pro Leu
1040 1045 1050

Gly Tyr Thr Gly Lys Asn Cys Gln Thr Leu Val Asn Leu Cys Ser
1055 1060 1065

Arg Ser Pro Cys Lys Asn Lys Gly Thr Cys Val Gln Lys Lys Ala
1070 1075 1080

Glu Ser Gln Cys Leu Cys Pro Ser Gly Trp Ala Gly Ala Tyr Cys
1085 1090 1095

Asp Val Pro Asn Val Ser Cys Asp Ile Ala Ala Ser Arg Arg Gly
1100 1105 1110

Val Leu Val Glu His Leu Cys Gln His Ser Gly Val Cys Ile Asn
1115 1120 1125

Ala Gly Asn Thr His Tyr Cys Gln Cys Pro Leu Gly Tyr Thr Gly
1130 1135 1140

Ser Tyr Cys Glu Glu Gln Leu Asp Glu Cys Ala Ser Asn Pro Cys
1145 1150 1155

Gln His Gly Ala Thr Cys Ser Asp Phe Ile Gly Gly Tyr Arg Cys
1160 1165 1170

Glu Cys Val Pro Gly Tyr Gln Gly Val Asn Cys Glu Tyr Glu Val
1175 1180 1185

Asp Glu Cys Gln Asn Gln Pro Cys Gln Asn Gly Gly Thr Cys Ile
1190 1195 1200

Asp Leu Val Asn His Phe Lys Cys Ser Cys Pro Pro Gly Thr Arg
1205 1210 1215

Gly Leu Leu Cys Glu Glu Asn Ile Asp Asp Cys Ala Arg Gly Pro
1220 1225 1230

His Cys Leu Asn Gly Gly Gln Cys Met Asp Arg Ile Gly Gly Tyr
1235 1240 1245

Ser Cys Arg Cys Leu Pro Gly Phe Ala Gly Glu Arg Cys Glu Gly
1250 1255 1260

Asp Ile Asn Glu Cys Leu Ser Asn Pro Cys Ser Ser Glu Gly Ser
1265 1270 1275

Leu Asp Cys Ile Gln Leu Thr Asn Asp Tyr Leu Cys Val Cys Arg
1280 1285 1290

Ser Ala Phe Thr Gly Arg His Cys Glu Thr Phe Val Asp Val Cys
1295 1300 1305

Pro Gln Met Pro Cys Leu Asn Gly Gly Thr Cys Ala Val Ala Ser
1310 1315 1320

Asn Met Pro Asp Gly Phe Ile Cys Arg Cys Pro Pro Gly Phe Ser
1325 1330 1335

Gly Ala Arg Cys Gln Ser Ser Cys Gly Gln Val Lys Cys Arg Lys
1340 1345 1350

Gly Glu Gln Cys Val His Thr Ala Ser Gly Pro Arg Cys Phe Cys
1355 1360 1365

Pro Ser Pro Arg Asp Cys Glu Ser Gly Cys Ala Ser Ser Pro Cys
1370 1375 1380

Gln His Gly Gly Ser Cys His Pro Gln Arg Gln Pro Pro Tyr Tyr
1385 1390 1395

Ser Cys Gln Cys Ala Pro Pro Phe Ser Gly Ser Arg Cys Glu Leu
1400 1405 1410

Tyr Thr Ala Pro Pro Ser Thr Pro Pro Ala Thr Cys Leu Ser Gln
1415 1420 1425

Tyr Cys Ala Asp Lys Ala Arg Asp Gly Val Cys Asp Glu Ala Cys
1430 1435 1440

Asn Ser His Ala Cys Gln Trp Asp Gly Gly Asp Cys Ser Leu Thr
1445 1450 1455

Met Glu Asn Pro Trp Ala Asn Cys Ser Ser Pro Leu Pro Cys Trp
1460 1465 1470

Asp Tyr Ile Asn Asn Gln Cys Asp Glu Leu Cys Asn Thr Val Glu
1475 1480 1485

Cys Leu Phe Asp Asn Phe Glu Cys Gln Gly Asn Ser Lys Thr Cys
1490 1495 1500

Lys Tyr Asp Lys Tyr Cys Ala Asp His Phe Lys Asp Asn His Cys
1505 1510 1515

Asn Gln Gly Cys Asn Ser Glu Glu Cys Gly Trp Asp Gly Leu Asp
1520 1525 1530

Cys Ala Ala Asp Gln Pro Glu Asn Leu Ala Glu Gly Thr Leu Val
1535 1540 1545

Ile Val Val Leu Met Pro Pro Glu Gln Leu Leu Gln Asp Ala Arg
1550 1555 1560

Ser Phe Leu Arg Ala Leu Gly Thr Leu Leu His Thr Asn Leu Arg
1565 1570 1575

Ile Lys Arg Asp Ser Gln Gly Glu Leu Met Val Tyr Pro Tyr Tyr
1580 1585 1590

Gly Glu Lys Ser Ala Ala Met Lys Lys Gln Arg Met Thr Arg Arg
1595 1600 1605

Ser Leu Pro Gly Glu Gln Glu Gln Glu Val Ala Gly Ser Lys Val
1610 1615 1620

Phe Leu Glu Ile Asp Asn Arg Gln Cys Val Gln Asp Ser Asp His

1625					1630					1635				
Cys	Phe	Lys	Asn	Thr	Asp	Ala	Ala	Ala	Ala	Leu	Leu	Ala	Ser	His
1640					1645					1650				
Ala	Ile	Gln	Gly	Thr	Leu	Ser	Tyr	Pro	Leu	Val	Ser	Val	Val	Ser
1655					1660					1665				
Glu	Ser	Leu	Thr	Pro	Glu	Arg	Thr	Gln	Leu	Leu	Tyr	Leu	Leu	Ala
1670					1675					1680				
Val	Ala	Val	Val	Ile	Ile	Leu	Phe	Ile	Ile	Leu	Leu	Gly	Val	Ile
1685					1690					1695				
Met	Ala	Lys	Arg	Lys	Arg	Lys	His	Gly	Ser	Leu	Trp	Leu	Pro	Glu
1700					1705					1710				
Gly	Phe	Thr	Leu	Arg	Arg	Asp	Ala	Ser	Asn	His	Lys	Arg	Arg	Glu
1715					1720					1725				
Pro	Val	Gly	Gln	Asp	Ala	Val	Gly	Leu	Lys	Asn	Leu	Ser	Val	Gln
1730					1735					1740				
Val	Ser	Glu	Ala	Asn	Leu	Ile	Gly	Thr	Gly	Thr	Ser	Glu	His	Trp
1745					1750					1755				
Val	Asp	Asp	Glu	Gly	Pro	Gln	Pro	Lys	Lys	Val	Lys	Ala	Glu	Asp
1760					1765					1770				
Glu	Ala	Leu	Leu	Ser	Glu	Glu	Asp	Asp	Pro	Ile	Asp	Arg	Arg	Pro
1775					1780					1785				
Trp	Thr	Gln	Gln	His	Leu	Glu	Ala	Ala	Asp	Ile	Arg	Arg	Thr	Pro
1790					1795					1800				
Ser	Leu	Ala	Leu	Thr	Pro	Pro	Gln	Ala	Glu	Gln	Glu	Val	Asp	Val
1805					1810					1815				
Leu	Asp	Val	Asn	Val	Arg	Gly	Pro	Asp	Gly	Cys	Thr	Pro	Leu	Met
1820					1825					1830				
Leu	Ala	Ser	Leu	Arg	Gly	Gly	Ser	Ser	Asp	Leu	Ser	Asp	Glu	Asp
1835					1840					1845				

Glu Asp Ala Glu Asp Ser Ser Ala Asn Ile Ile Thr Asp Leu Val
1850 1855 1860

Tyr Gln Gly Ala Ser Leu Gln Ala Gln Thr Asp Arg Thr Gly Glu
1865 1870 1875

Met Ala Leu His Leu Ala Ala Arg Tyr Ser Arg Ala Asp Ala Ala
1880 1885 1890

Lys Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn Ala Gln Asp Asn
1895 1900 1905

Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala Asp Ala Gln
1910 1915 1920

Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Val Thr Asp Leu Asp
1925 1930 1935

Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala Arg
1940 1945 1950

Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala
1955 1960 1965

Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp
1970 1975 1980

Ala Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Leu Lys
1985 1990 1995

Asn Gly Ala Asn Arg Asp Met Gln Asp Asn Lys Glu Glu Thr Pro
2000 2005 2010

Leu Phe Leu Ala Ala Arg Glu Gly Ser Tyr Glu Ala Ala Lys Ile
2015 2020 2025

Leu Leu Asp His Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp
2030 2035 2040

Arg Leu Pro Arg Asp Val Ala Arg Asp Arg Met His His Asp Ile
2045 2050 2055

Val	Arg	Leu	Leu	Asp	Glu	Tyr	Asn	Val	Thr	Pro	Ser	Pro	Pro	Gly
2060						2065					2070			
Thr	Val	Leu	Thr	Ser	Ala	Leu	Ser	Pro	Val	Ile	Cys	Gly	Pro	Asn
2075						2080					2085			
Arg	Ser	Phe	Leu	Ser	Leu	Lys	His	Thr	Pro	Met	Gly	Lys	Lys	Ser
2090						2095					2100			
Arg	Arg	Pro	Ser	Ala	Lys	Ser	Thr	Met	Pro	Thr	Ser	Leu	Pro	Asn
2105						2110					2115			
Leu	Ala	Lys	Glu	Ala	Lys	Asp	Ala	Lys	Gly	Ser	Arg	Arg	Lys	Lys
2120						2125					2130			
Ser	Leu	Ser	Glu	Lys	Val	Gln	Leu	Ser	Glu	Ser	Ser	Val	Thr	Leu
2135						2140					2145			
Ser	Pro	Val	Asp	Ser	Leu	Glu	Ser	Pro	His	Thr	Tyr	Val	Ser	Asp
2150						2155					2160			
Thr	Thr	Ser	Ser	Pro	Met	Ile	Thr	Ser	Pro	Gly	Ile	Leu	Gln	Ala
2165						2170					2175			
Ser	Pro	Asn	Pro	Met	Leu	Ala	Thr	Ala	Ala	Pro	Pro	Ala	Pro	Val
2180						2185					2190			
His	Ala	Gln	His	Ala	Leu	Ser	Phe	Ser	Asn	Leu	His	Glu	Met	Gln
2195						2200					2205			
Pro	Leu	Ala	His	Gly	Ala	Ser	Thr	Val	Leu	Pro	Ser	Val	Ser	Gln
2210						2215					2220			
Leu	Leu	Ser	His	His	His	Ile	Val	Ser	Pro	Gly	Ser	Gly	Ser	Ala
2225						2230					2235			
Gly	Ser	Leu	Ser	Arg	Leu	His	Pro	Val	Pro	Val	Pro	Ala	Asp	Trp
2240						2245					2250			
Met	Asn	Arg	Met	Glu	Val	Asn	Glu	Thr	Gln	Tyr	Asn	Glu	Met	Phe
2255						2260					2265			

Gly Met Val Leu Ala Pro Ala Glu Gly Thr His Pro Gly Ile Ala
2270 2275 2280

Pro Gln Ser Arg Pro Pro Glu Gly Lys His Ile Thr Thr Pro Arg
2285 2290 2295

Glu Pro Leu Pro Pro Ile Val Thr Phe Gln Leu Ile Pro Lys Gly
2300 2305 2310

Ser Ile Ala Gln Pro Ala Gly Ala Pro Gln Pro Gln Ser Thr Cys
2315 2320 2325

Pro Pro Ala Val Ala Gly Pro Leu Pro Thr Met Tyr Gln Ile Pro
2330 2335 2340

Glu Met Ala Arg Leu Pro Ser Val Ala Phe Pro Thr Ala Met Met
2345 2350 2355

Pro Gln Gln Asp Gly Gln Val Ala Gln Thr Ile Leu Pro Ala Tyr
2360 2365 2370

His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro Thr Pro Pro Ser
2375 2380 2385

Gln His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg Thr Pro Ser
2390 2395 2400

His Ser Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr Pro Ser
2405 2410 2415

Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Ser Pro His Ser Ala
2420 2425 2430

Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala
2435 2440 2445

Gly Gly Gly Gln Arg Gly Pro Gly Thr His Met Ser Glu Pro Pro
2450 2455 2460

His Asn Asn Met Gln Val Tyr Ala
2465 2470

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<211> 16

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<400> 13

Arg	Gln	Ile	Lys	Ile	Trp	Phe	Gln	Asn	Arg	Arg	Met	Lys	Trp	Lys	Lys
1				5					10					15	